PA VT COOPERATION TREAT

From	the	IN	TERN	ΙΔΙ	ION	IAL	RI.	IRF.	ΑI	u

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

LIGIII	uie	11.4	LEM	AV 1.1	CIAN	בטנ
-						
To:						

Commissioner
US Department of Commerce
United States Patent and Trademark
Office, PCT
2011 South Clark Place Room
CP2/5C24
Arlington, VA 22202

Date of mailing (day/month/year) 02 March 2001 (02.03.01)	in its capacity as elected Office				
International application No. PCT/US00/18345	Applicant's or agent's file reference A0000102-01E				
International filing date (day/month/year) 05 July 2000 (05.07.00)	Priority date (day/month/year) 16 July 1999 (16.07.99)				
Applicant BARRETT, Stephen, Douglas et al					

1.	The designated Office is hereby notified of its election made:
	X in the demand filed with the International Preliminary Examining Authority on:
	18 January 2001 (18.01.01)
	in a notice effecting later election filed with the International Bureau on:
2.	The election X was
	was not
	made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland **Authorized officer**

Zakaria EL KHODARY

Telephone No.: (41-22) 338.83.38

PATENT COOPERATION TREATY

A0000103

From the INTERNATIONAL PRELIMINAR		AMINING AUTHORITY	- J	istit	i Shbrook
To:					PCT
Warner-Lambert Company Legal Division c/o Gödecke AG, Patents Mooswaldallee 1 D-79090 Freiburg ALLEMAGNE	Eing	Patentweser		THE INT	ATION OF TRANSMITTAL OF ERNATIONAL PRELIMINARY KAMINATION REPORT (PCT Rule 71.1)
	<u> </u>		Date of the control o	nailing nth/year)	07.08.2001
Applicant's or agent's file reference A0000102-01E				II.	MPORTANT NOTIFICATION
International application No. PCT/US00/18345		International filing date (da 05/07/2000	ay/month/y	rear)	Priority date (day/month/year) 16/07/1999
Applicant WARNER AMBERT COMP	NIV				

- 1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
- 2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
- 3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

Authorized officer

9))

European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465

Senkel, H

Tel.+49 89 2399-8071





INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

1 ''	_	nt's file reference	FOR FURTHER AC	TION		ion of Transmittal of International
A000010	2-01	E	PON PONTILE AG		Preliminary E	Examination Report (Form PCT/IPEA/416)
Internationa	ıl appli	cation No.	International filing date (da	ay/month/y	ear)	Priority date (day/month/year)
PCT/US0	0/18	345	05/07/2000			16/07/1999
Internationa A61K31/0		nt Classification (IPC) or na	tional classification and IPC			
Applicant					-	
WARNER	R-LAI	MBERT COMPANY		 .		
		ational preliminary exame smitted to the applicant a		repared b	y this Interr	national Preliminary Examining Authority
2. This F	REPO	RT consists of a total of	7 sheets, including this	cover she	et.	
bo (s	een a ee R	mended and are the bas	sis for this report and/or s 07 of the Administrative I	sheets cor	ntaining rect	claims and/or drawings which have ifications made before this Authority PCT).
·		· · · · · · · · · · · · · · · · · · ·				
3. This re	eport	contains indications rela	ting to the following item	s:		
ı	X	Basis of the report			•	
11		Priority				·
111	X	Non-establishment of o	pinion with regard to nov	elty, inver	ntive step ar	nd industrial applicability
١٧		Lack of unity of invention	on .			
V.	×		nder Article 35(2) with reg ons suporting such staten		velty, inven	tive step or industrial applicability;
VI	×	Certain documents cite	ed ·			
VII		Certain defects in the in	nternational application		٠	
VIII	⊠	Certain observations or	n the international applica	ation		
Date of sub	missio	n of the demand		Date of cor	npletion of thi	s report
18/01/200	01			07.08.200 1	.	
	exami	address of the international ning authority:		Authorized	officer	
6)))	D-80	pean Patent Office 298 Munich		Büttner, I	U	
		+49 89 2399 - 0 Tx: 523656 +49 89 2399 - 4465	· i	Telephone	No. +49 89 2	399 7841

International application No. PCT/US00/18345

I. Bas	is of ti	h ri	port
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1.	the and	Vith regard to the elements of the int mational application (Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)): Description, pages:							
	1-7	1	as originally filed						
	Cla	ims, No.:							
									
	1-3	2	as originally filed						
	Dra	wings, sheets:							
	1/8-	-8/8	as originally filed						
	•								
2.			guage, all the elements marked above were available or furnished to this Authority in th international application was filed, unless otherwise indicated under this item.						
	The	ese elements were a	available or furnished to this Authority in the following language: , which is:						
		the language of a	translation furnished for the purposes of the international search (under Rule 23.1(b)).						
		the language of pu	ublication of the international application (under Rule 48.3(b)).						
		the language of a 55.2 and/or 55.3).	translation furnished for the purposes of international preliminary examination (under Rule						
3.			electide and/or amino acid sequence disclosed in the international application, the yexamination was carried out on the basis of the sequence listing:						
		contained in the in	iternational application in written form.						
		filed together with	the international application in computer readable form.						
		fumished subsequ	ently to this Authority in written form.						
		furnished subsequ	ently to this Authority in computer readable form.						
			t the subsequently furnished written sequence listing does not go beyond the disclosure in pplication as filed has been furnished.						
		The statement tha listing has been fu	t the information recorded in computer readable form is identical to the written sequence mished.						
4.	The	amendments have	resulted in the cancellation of:						
		the description,	pages:						
		the claims,	Nos.:						



		the drawings,	sheets:	
5.		This report has been considered to go be	established as if (some of) the amendments had not been made, since they have be ond the disclosure as filed (Rule 70.2(c)):	∍e
		(Any replacement st report.)	eet containing such amendments must be referred to under item 1 and annexed to the	ગાં
6.	Add	litional observations,	necessary:	
III.	Nor	n-establishment of o	pinion with regard to novelty, inventive step and industrial applicability	•
1.	The obv	e questions whether the rious), or to be industr	e claimed invention appears to be novel, to involve an inventive step (to be non- ally applicable have not been examined in respect of:	
		the entire internation	al application.	
	×	claims Nos. 1-32 wit	respect to industrial applicability.	
be	caus	Se:		
	Ø	the said international does not require an see separate sheet	application, or the said claims Nos. 1-32 relate to the following subject matter which nternational preliminary examination (<i>specify</i>):	
			s or drawings (<i>indicate particular elements below</i>) or said claims Nos. are so unclea pinion could be formed (<i>specify</i>):	ır
		the claims, or said claims, or said claims, or said claims.	aims Nos. are so inadequately supported by the description that no meaningful opini	O I
		no international sear	ch report has been established for the said claims Nos	
2.	and	neaningful internationa Vor amino acid seque tructions:	I preliminary examination cannot be carried out due to the failure of the nucleotide ace listing to comply with the standard provided for in Annex C of the Administrative	
٠		the written form has	not been furnished or does not comply with the standard.	
		the computer readal	le form has not been furnished or does not comply with the standard.	
V.			der Article 35(2) with regard to novelty, inventive step or industrial applicability ns supporting such statement	/ ;
1.	Sta	tement		
	Nov	velty (N)	Yes: Claims 1-32	

International application No. PCT/US00/18345

No:

Claims

Inventive step (IS)

Yes:

Claims 1-32 Claims

No: Industrial applicability (IA) Yes

Yes: C

Claims see section III

No: Claims

2. Citations and explanations see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made: see separate sheet

R It m III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 1-21 and 23-32 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Item V

Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The following International Preliminary Examination has been carried out on the assumption that the present application is fully entitled to its priority date as claimed.

Prior Art

Reference is made to the following document:

D1: WO 9901421 A

The document D1 is not cited in the international search report.

Claims 1-21 and 23-32

(N) Claim 1 describes a method for treating chronic pain by administration of compounds following formula (I) of claim 1.

D1 discloses compounds with a structure similar to the claimed compounds. The present application differs in the cyclic ring described as formula Z in the present application.

Therefore the subject matter of claim 1 is novel.

Thus also the subject matter of claims 2-21 and 23-32 is novel.

(IS) D1, which is considered to represent the most relevant state of the art, disclos s

MEK-inhibitors for treatment of cancer (D1, P7 L7, claim 26), diab tes (D1, P7 L7, claim 31) and inflammation (D1, Abstract).

According to the description of the present application cancer (P1, L31), diabetes (P1, L14) and inflammation (claim 4) are associated with neuropathic pain.

The present application differs from D1 in the radical (Z). No indication can be found in the prior art to introduce this group Z into the compounds disclosed in D1. Consequently the subject matter of claim 1 is inventive.

Claims 2-21 and 23-32 are dependent on claim 1 and as such also meet the requirements of the PCT with respect to inventive step (Article 33(3) PCT).

(IA) For the assessment of the present claims 1-21 23-32 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

Claim 22

(N)(IS)

The compounds described in claim 22 are not disclosed in the prior art. The prior art also does not suggest these compounds for the treatment of chronic pain (see above paragraph). Therefore the subject matter of claim 22 is new and inventive.

Re Item VI

Certain documents cited

The following document is not considered to be part of the prior art (Rule 64.3 PCT). It claims priority of 13.01.1999 and 02.03.1999, has been filed 21.12.1999 and was published 20.07.2000.

D2: WO 00 42022 A

D2 discloses the use of compounds following formula (I) for the treatment of

different types of arthritis (D2; Claims 32 and 33). According to the description of the present application (P1, L18) diseases associated with neuropathic pain include arthritis.

Furthermore D2 discloses compounds described in product claim 22. (see D2 claim 14).

In case the present application would enter the European Phase the abovementioned document, which is cited in the ISR, would be prejudicial to the novelty of the subject matter of claims 1-4 and 7-32 of the present application.

Re Item VIII

Certain observations on the international application

Formulas presented in schemes 7-9 (P24-26) are not comprised in the claims (R₃ and R_{4} are mixed up).

The content of biological examples 1 and 2 (P41-46) does not fall within the scope of the claimed subject matter (Article 6 PCT).

Dependent method claims 2-21 and 23 -32 are not grouped together (Rule 6.4 (c) PCT).

Compound PD297447 (P47) could not be identified.



PCT From the INTERNATIONAL SEARCHING AUTHORITY To: NOTIFICATION OF TRANSMITTAL OF WARNER-LAMBERT COMPANY THE INTERNATIONAL SEARCH REPORT Attn. RYAN, M. Andrea OR THE DECLARATION 201 Tabor Road NOTED 07950 Morris Plains, New Jersey (PCT Rule 44.1) UNITED STATES OF AMERICA JAN 29 208097 K. STRITENBERGER Date of mailing (day/month/year) 23/01/2001 Applicant's or agent's file reference See paragraphs 1 and 4 below FOR FURTHER ACTION A0000102-01E International application No. International filing date (day/month/year) 05/07/2000 PCT/US 00/18345 Applicant WARNER-LAMBERT COMPANY The applicant is hereby notified that the International Search Report has been established and is transmitted herewith. Filing of amendments and statement under Article 19: The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46): The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet. International Bureau of WIPO Where? Directly to the 34, chemin des Colombettes 1211 Geneva 20, Switzerland Fascimile No.: (41-22) 740.14.35 For more detailed instructions, see the notes on the accompanying sheet. The applicant is hereby notified that no International Search Report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith. With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that: the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices. no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made. 4. Further action(s): The applicant is reminded of the following: Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90bis.1 and 90bis.3, respectively, before the completion of the technical preparations for international publication. Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later). Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2

NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,

priority dat or could not be elect d because they are not bound by Chapter II.

Fax: (+31-70) 340-3016

Authorized offic r

before all designated Offices which have not been elected in the demand or in a later election within 19 months from the

Joannes Vergoosen

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international politication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When?

Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been its filed, see below.

How?

Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (ntinued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

- [Where originally there were 48 claims and after amendment of some claims there are 51]:
 *Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers;
 claims 30, 33 and 36 unchanged; new claims 49 to 51 added.*
- [Where originally there were 15 claims and after amendment of all claims there are 11]:
 "Claims 1 to 15 replaced by amended claims 1 to 11."
- 3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]: "Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or "Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
- [Where various kinds of amendments are made]:
 "Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claims 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

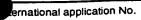
For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.



INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	FOR FURTHER see Notification of (Form PCT/ISA/2	of Transmittal of International Search Report 220) as well as, where applicable, item 5 below.
A0000102-01E	ACTION	·
International application No.	International filing date (day/month/year)	(Earliest) Priority Date (day/month/year)
PCT/US 00/18345	05/07/2000	16/07/1999
Applicant	-	
WARNER-LAMBERT COMPANY		
This International Search Report has be according to Article 18. A copy is being	en prepared by this International Searching Autransmitted to the International Bureau.	thority and is transmitted to the applicant
This International Search Report consis	ts of a total of sheets. by a copy of each prior art document cited in thi	s report.
Basis of the report		the state of the s
a. With regard to the language , the language in which it was filed, to	e international search was carried out on the banks otherwise indicated under this item.	asis of the international application in the
Authority (Rule 23.1(b))	was carried out on the basis of a translation of	
b. With regard to any nucleotide was carried out on the basis of	and/or amino acid sequence disclosed in the	international application, the international search
contained in the internal	tional application in written form.	,
filed together with the in	nternational application in computer readable fo	rm.
furnished subsequently	to this Authority in written form.	
furnished subsequently	to this Authority in computer readble form.	
international application	subsequently furnished written sequence listing n as filed has been furnished.	
the statement that the i furnished	nformation recorded in computer readable form	n is identical to the written sequence listing has beer
2. Certain claims were f	ound unsearchable (See Box I).	
3. Unity of invention is		
4. With regard to the title,		
	submitted by the applicant.	
	blished by this Authority to read as follows:	•
5. With regard to the abstract,		
	s submitt d by the applicant. blished, according to Rule 38.2(b), by this Auth the date of mailing of this international search	ority as it app ars in Box III. The applicant may, report, submit comments to this Authority.
	published with the abstract is Figure No.	· ·
as suggested by the a		None of the figures.
	fail d to suggest a figure.	
	tter characterizes the inv ntion.	



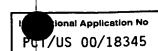
INTERNATIONAL SEARCH REPORT

PCT/US 00/18345

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 	O	\sim \sim \sim \sim \sim	'/Cantinuation	OT IT	m 5 of the firs	SISHEED

formula (I) shown	in claim 1 of the ap	pricacion.		
				•
		•		
	,			
			•	

INTERMITIONAL SEARCH REPORT



A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K31/404 A61K31/4192 A61K31/4245 A61K31/433 A61K31/42 A61K31/498 A61P25/04 A61K31/428

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

 $\label{lem:minimum documentation searched (classification system followed by classification symbols)} IPC~7~A61K$

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
E	WO 00 42022 A (BARRETT STEPHEN DOUGLAS; BRIDGES ALEXANDER JAMES (US); WARNER LAMB) 20 July 2000 (2000-07-20) cited in the application claims; examples	22
A	WO 98 37881 A (BRIDGES ALEXANDER JAMES; WARNER LAMBERT CO (US)) 3 September 1998 (1998-09-03) the whole document	1-32
	-/	

Further documents are listed in the continuation of box C.	X ratem lamby the moore are noted in a moore
Special categories of cited documents: A* document defining the general state of the art which is not considered to be of particular relevance	*T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
E earlier document but published on or after the international filing date	"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
 L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) *O* document referring to an oral disclosure, use, exhibition or other means *P* document published prior to the international filing date but later than the priority date claimed 	 "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. "&" document member of the same patent family
Date of the actual completion of the international search	Date of mailing of the international search report
12 January 2001	23/01/2001
Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk	Authorized officer
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Veronese, A

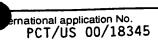
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Category ° Cita	BEKEMEIER H ET AL: "STRUCTURE-ACTIVITY RELATIONSHIP IN NONSTEROIDAL ANTIINFLAMMATORY AGENTS, INCLUDING OSAR IN FENAMATE DERIVATIVES" AGENTS AND ACTIONS SUPPLEMENTS, CH, BIRKHAEUSER VERLAG, BASEL, 1 July 1982 (1982-07-01), pages 17-34, XP002063635 ISSN: 0379-0363 the whole document DUNCIA J V ET AL: "MEK inhibitors: the chemistry and biological activity of U0126, its analogs, and cyclization products" BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, GB, OXFORD, vol. 8, no. 20, 20 October 1998 (1998-10-20), pages 2839-2844, XP004139571 ISSN: 0960-894X the whole document	1-32
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INTERNATIONAL SEARCH REPORT



Box I Observations where certain claims were found unsearchabl (Continuation of item 1 of first sheet)
This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:
1. X Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: Although claims 1-21, 23-32 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).
Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)
This International Searching Authority found multiple inventions in this international application, as follows:
As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
Remark on Protest The additional search fees were accompanied by the applicant's protest. No protest accompanied the payment of additional search fees.

Information on patent family members

ional Application No
PCT/US 00/18345

Information on patent			101,00	
Patent document	Publication	Patent family memb r(S)		Publication date
cited in search r port WO 0042022	date 20-07-2000	AU 2203 JP 2000204	700 A 079 A	01-08-2000 25-07-2000
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 Without international search report and to be republished upon receipt of that report.

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